5. (Amended) The labeled probe molecules of claim 1 wherein the nucleotides are nucleotide analogs including 2-amino purine for adenosine or guanine; ribonucleoside or 2,6-diamino ribonucleoside, formycin A, formycin B, oxyformycin B, toyocamycin, sangivamycin, pseudoouridine, showdomycin, minimycin, pyrazomycin, 5-amino-formycin A, 5-amino-formycin B or 5-oxo-formycin A for adenosine; 4-amino-pyrazolo [3,4d] pyrimidine, 4,6-diamino-pyrazolo [3,4d] pyrimidine, 4-oxo-pyrazolo [3,4d] pyrimidine; 4-oxo-6-amino-pyrazolo [3,4d] pyrimidine, 4,6-dioxo-pyrazolo [3,4d] pyrimidine, pyrazolo [3,4d] pyrimidine, 6-amino-pyrazolo [3,4d] pyrimidine or 6-oxo-pyrazolo [3,4d] pyrimidine for cytosine or thymidine.

17. (Amended) A method for quantifying the amount of a target molecule in solution comprising the steps of:

a. procuring a first substrate having a surface area comprising a known number of labeled probe molecules;

b. detecting a first level of label expressed by the labeled probe molecules on the first substrate;

c. contacting the first substrate with a volume of sample containing unlabeled target nucleotide sequences;

d. providing sufficient conditions and time for unlabeled target molecules to selectively pair with the labeled probe molecules;

e. removing the first substrate and detecting the level of label expressed by the substrate after exposure to the sample containing unlabeled target molecules;

f. where the level of label expression of the first substrate is substantially reduced to levels substantially similar to background levels, repeating steps a. through e. with subsequent substrates, having surface areas comprising known numbers of labeled probe molecules.

g. calculating the amount of target molecule in the volume of sample by adding the known number of labeled probe molecules present on the first substrate and subsequent

substrates contacted with the sample, wherein the levels of label expression of the substrates were reduced relative to the levels prior to contacting the sample.

22. (Amended) A method for monitoring the hybridization of a probe and a target comprising supplying a fluorescently labeled probe providing a detectable first level of fluorescence and providing a detectable second level of fluorescence when the labeled probe is hybridized to a complementary unlabeled target, wherein the second level is lower than the first level.

23. (Amended) A method for monitoring the hybridization of a probe and a target comprising supplying a fluorescently labeled probe providing a detectable first level of fluorescence, and providing a detectable second level of fluorescence when the labeled probe is hybridized to a complementary unlabeled target, wherein the second level is significantly lower than the first level.

24. (Amended) A method for monitoring the hybridization of a probe and a target comprising supplying a fluorescently labeled probe providing a detectable first level of fluorescence, and providing a detectable second level of fluorescence when the labeled probe is hybridized to a complementary unlabeled target, wherein the second level is approximately zero.

25. (Amended) A method for monitoring the hybridization of a probe and a target comprising supplying a fluorescently labeled probe providing a detectable first level of fluorescence, and a detectable second level of fluorescence when the labeled probe is hybridized to a complementary unlabeled target, wherein the second level is approximately zero and the first level is greater than zero.

27. (Amended) A substrate having a plurality of probes, wherein said probes are fluorescently labeled, the labeled probe providing a detectable first level of fluorescence, and when hybridized to a complementary target providing a second level of fluorescence, wherein the second level is lower than the first level.

28. (Amended) A substrate having a plurality of probes, wherein said probes are fluorescently labeled, the labeled probe providing a detectable first level of fluorescence, and

when hybridized to a complementary target providing a second level of fluorescence, wherein the second level is significantly lower than the first level.

29. (Amended) A substrate having a plurality of probes, wherein said probes are fluorescently labeled, the labeled probe providing a detectable first level of fluorescence, and when hybridized to a complementary target providing a second level of fluorescence, wherein the second level approaches zero.

30. (Amended) A substrate having a plurality of probes, wherein said probes are fluorescently labeled, the labeled probe providing a detectable first level of fluorescence, and when hybridized to a complementary target providing a second level of fluorescence, wherein the second level is greater than zero.

33. (Added) A method of labeling or modifying a probe by incorporating an analog nucleotide.

34. (Added) The method of claim 31 whereby the labeled probe molecules are nucleotide analogs including 2 –amino purine for adenosine or guanine; ribonucleoside or 2,6-diamino ribonucleoside, formycin A, formycin B, oxyformycin B, toyocamycin, sangivamycin, pseudoouridine, showdomycin, minimycin, pyrazomycin, 5-amino-formycin A, 5-amino-formycin B or 5-oxo-formycin A for adenosine; 4-amino-pyrazolo [3,4d] pyrimidine, 4,6-diamino-pyrazolo [3,4d] pyrimidine, 4-amino-6-oxo-pyrazolo [3,4d] pyrimidine, 4-oxo-pyrazolo [3,4d] pyrimidine, 4-oxo-6-amino-pyrazolo [3,4d] pyrimidine, 4,6-dioxo-pyrazolo [3,4d] pyrimidine, pyrazolo [3,4d] pyrimidine, 6-amino-pyrazolo [3,4d] pyrimidine or 6-oxo-pyrazolo [3, 4d] pyrimidine for cytosine or thymidine.

35. (Added) The method of claim 31 whereby the incorporated nucleotide analog is 2-aminopurine replacing adenosine or guanine nucleotides.

36. (Added) The method of claim 33 whereby after incorporation of the nucleotide analog including 2-aminopurine, the labeled probe is affixed on a solid substrate.

37. (Added) The method for quantifying the amount of a target molecule in solution comprising the steps of:

a. incorporating a nucleotide analog including 2-aminopurine into a probe;

b. affixing the labeled or modified probe on a substrate;

c. detecting a first level of label expressed by the labeled or modified probe molecules on the substrate;

d. contacting substrate with a volume of sample containing unlabeled or unmodified target molecules in solution;

e. providing sufficient conditions and time for unlabeled or unmodified target molecules in solution to selectively pair and hybridize with the labeled probe molecules affixed on the substrate;

f. removing the substrate and detecting the second level of label expressed by the labeled probed affixed on the substrate after exposure to the unlabeled or unmodified target molecules in solution;

g. comparing the first and second levels of label expressed by the labeled or modified probe;

h. identifying probe and target hybridized molecules by repeating steps c-f until the amounts of label expression between the first and second levels of label approaches zero and/or about background levels.

REMARKS

I. PRELIMINARY REMARKS

Applicant has carefully considered the detailed Office Action and sets forth detailed responses herein. Applicant has amended specific claims addressed by the Examiner in the Office Action dated October 3, 2001.

This Supplemental Amendment is meant to supplement the Amendment filed by facsimile on February 1, 2002. The only difference between this Supplemental Amendment and the